REMARKS

The Official Action dated April 24, 2006 has been carefully considered. Accordingly, the amendments presented herewith, taken with the following remarks, are believed sufficient to place the present application in condition for allowance. Reconsideration is respectfully requested.

By the present amendment, claim 1 has been amended to delete the word "protozoan". It is believed that this change does not involve any introduction of new matter, whereby entry is believed to be in order and is respectfully requested.

In the Official Action, the Examiner has asserted that claims 6-9, 11-12, 14-16, 20 and 21 have been withdrawn from further consideration as being drawn to non-elected species, there being no allowable generic or linking claim. However, Applicant's Response dated February 2, 2006 to the Restriction Requirement specifically stated that claims 1-4 and 16-19 were generic, as previously asserted by the Examiner, and therefore, upon allowance of a generic claim, Applicants submit that the additional species recited in claims 6-9, 11-12, 14-16, 20 and 21 will be entitled to consideration.

Claims 1-5, 10, 13 and 17-19 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner asserted that the claims have no written support in the specification for the broad genus "LPS derived from microbial, protozoan and/or fungal endotoxin," but only have support for "LPS derived from *E. coli* bacteria". Applicants traverse this rejection. However, to expedite prosecution of this application, claim 1 has been amended to delete the word "protozoan". In addition, Applicants submit that LPS derived from microbial and/or fungal endotoxin are similar in structure and further submit that LPS derived from gram negative bacteria, such as *E. coli* bacteria, is a representative species of the entire genus of LPS derived from microbial and/or fungal endotoxins. Specifically, to support these assertions, Applicants refer to the teachings of Knirel YA et al. "Structural *features and structural variability of the lipopolysaccaride of Yersinia pestis, the cause of plague". J. Endotoxin Res.* 2006: 12, 3-9, which disclose the structural similarities of fungal and bacterial LPS and the teachings of Trent MS. "Biosynthesis, transport, and modification of lipid A". *Biochem Cell Biol.* 2004 Feb;82(1):71-86. Review (enclosed herewith), which discloses that gram-negative bacteria in general have very similar LPS structural properties. A copy of the Knierl YA et al reference will be submitted in a

supplemental response. Accordingly, it is therefore submitted that the evidence presented herewith demonstrate that the specification's disclosure of LPS derived from *E. coli* provides sufficient support for the broad genus of LPS derived from microbial and/or fungi endotoxin.

Claims 1-5, 10 and 17-19 were rejected under 35 U.S.C. §103(a) as being obvious and therefore unpatentable over Tulic et al, *Am. J. Resp. Cell Mol. Biol.*, Vol. 22, pp. 604-612, 2000 in view of Matricardi et al, "Microbial Products in Allergy Prevention and Therapy", *Allergy*, 2003:58:pp. 461-471 and Bertók, "Stimulation of Nonspecific Resistance By Radiation-Detoxified Endotoxin", *Beneficial Effects of Endotoxins*, Plenum Publishing Corp., 1983, pp. 213-226. The Examiner asserted that Tulic et al teach the prevention of allergy in 10-day old, immature mice administered LPS in aerosol, however, Tulic et al fail to teach the administration of irradiated LPS to the mammals. The Examiner asserted that Matricardi et al teach the administration of LPS has been shown to be beneficial to treat allergy, however, a less toxic derivative of LPS would be preferred for treatment purposes. The Examiner asserted that Bertók teaches making irradiated LPS, which is a less toxic form of LPS that still stimulates an immune response, however Bertók is silent as to the type of immune response. Accordingly, the Examiner asserted that one of ordinary skill in the art would have been motivated to treat the mammals of Tulic et al with the irradiated LPS molecules of Bertók because the irradiated LPS molecule is less toxic but maintains its immunostimulatory properties as taught by Matricardi et al.

However, as will be set forth in detail below, Applicants submit that the processes defined by claims 1-5, 10 and 17-19 are nonobvious over and patentably distinguishable from Tulic et al in view of Matricardi et al and Bertók. Accordingly, this rejection is traversed and reconsideration is respectfully requested.

Particularly, claim 1 recites a process for inhibiting development of allergic disease. The process comprises exposing a neonatal or immature mammal or bird to irradiation-detoxified lipopolysaccharide derived from microbial and/or fungal endotoxin.

Applicants submit that the combination of references does not teach, suggest or recognize the use of irradiated-LPS in a neonatal or immature mammal or bird for inhibiting the development of allergic disease. Tulic et al teach modification of the inflammatory response in adult 10-week old mice. See page 604, column 2 under Materials and Methods - Animals. In contrast, the present invention is directed to processes for inhibiting development of allergic

disease comprising exposing a neonatal or immature mammal or bird to irradiation-detoxified lipopolysaccharide derived from microbial and/or fungal endotoxin. The specification of the present invention at page 2, lines 23-25 further defines "immature" as a mammal or bird which has not completed life cycle development to its adult stage. Thus, the teachings of Tulic et al of the modification of the inflammatory response in adult 10-week old mice does not teach, suggest or recognize processes for inhibiting the development of allergic disease in a neonatal or immature mammal or bird as required by the claims.

Moreover, as asserted by the Examiner, Tulic et al and Matricardi et al fail to teach the administration of irradiated LPS to inhibit development of allergic disease in a mammal as defined by the claims. The deficiencies of Tulic et al and Matricardi et al are not overcome by the teachings of Bertók. Specifically, Bertók discloses the use of detoxified LPS in the pretreatment in various shocks, radiation diseases and infections. However, Bertók fails to disclose that irradiated-LPS can be used to inhibit the development of allergic disease or that irradiated-LPS maintains immune stimulating anti-allergic properties. Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention absent some teaching, suggestion or incentive supporting the combination, *In re Geiger*, 2 U.S.P.Q. 2d 1276 (Fed. Cir. 1987). The Examiner must give some reason as to why one of ordinary skill in the art would have been prompted to combine the teachings of the cited references to arrive at the claimed invention since it is the burden of the Examiner to establish a *prima facie* case of obviousness. The Examiner cannot pick and choose among the individual elements of assorted prior art references to recreate the claimed invention; the Examiner has the burden to show some teaching or suggestion in the references to support their use in the particular claimed combination, *Smith-Kline Diagnostics, Inc. v. Helena Laboratories Corp.*, 8 U.S.P.Q. 2d 1468, 1475 (Fed. Cir. 1988). Finally, both a suggestion to combine the references and a reasonable expectation of success must be found in the art itself for a proper prima facie case of obviousness, *In re Dow Chemical Co.*, 5 U.S.P.Q. 2d 1529 (Fed. Cir. 1988). Therefore, because the Bertók disclosures are directed to pretreatment in various shocks, radiation diseases and infections and Tulic et al and Matricardi are directed to allergy prevention, Applicants assert that there would be no motivation to combine Bertók with the Tulic et al and Matricardi to arrive at the claimed processes.

References relied upon to support a rejection under 35 U.S.C. §103 must provide an enabling disclosure, i.e., they must place the claimed invention in the possession of the public, *In*

re Payne, 203 U.S.P.Q. 245 (CCPA 1979). As noted above, Applicants find no teaching, suggestion or reference in Tulic et al in view of Matricardi et al and Bertók of the process for inhibiting development of allergic disease comprising exposing a neonatal or immature mammal or bird to irradiation-detoxified lipopolysaccharide derived from microbial and/or fungal endotoxin as recited by the claims. In addition, Applicants find no teaching, suggestion or reference in Tulic et al in view of Matricardi et al and Bertók for modifying the disclosures therein to arrive at the claimed invention. In view of the failure of Tulic et al in view of Matricardi et al and Bertók to teach, suggest or recognize the process for inhibiting development of allergic disease as recited by the claims, the references do not support a rejection of claims 1-5, 10 and 17-19 under 35 U.S.C. §103.

It is therefore submitted that the claimed processes as defined by claims 1-5, 10 and 17-19 are nonobvious over and patentably distinguishable from the teachings of Tulic et al in view of Matricardi et al and Bertók, whereby the rejection under 35 U.S.C. §103 has been overcome. Reconsideration is respectfully requested.

Claims 1 and 13 were rejected under 35 U.S.C. §103(a) as being unpatentable over Tulic et al in view of Matricardi et al and Bertók, as applied to claims 1-5, 10 and 17-19 above, and further in view of Liu et al, *Current Reviews of Allergy and Clinical Immunology*, Vol. 109, pp. 379-392, 2002. With respect to Liu et al, the Examiner asserted that Liu et al teach that there is ample data demonstrating that early life, less than two years, exposure to endotoxins, such as LPS, in humans has been demonstrated to decrease allergic sensitization and that frequent benign exposures to endotoxin early in life should be expected to influence immune development to prevent atopy, allergic disease and asthma. The Examiner asserted that one of ordinary skill in the art would have been motivated to use the treatment method taught by the combination of Tulic et al in view of Matricardi et al and Bertók to treat young humans since Liu et al recognize early exposures to LPS in a benign way should be effective in preventing allergy.

However, as will be set forth in detail below, Applicants submit that the processes defined by claims 1 and 13 are nonobvious over and patentably distinguishable from Tulic et al in view of Matricardi et al and Bertók, as applied to claims 1-5, 10 and 17-19 above, and further in view of Liu et al. Accordingly, this rejection is traversed and reconsideration is respectfully requested.

Particularly, as detailed above, claim 1 recites a process for inhibiting development of allergic disease comprising exposing a neonatal or immature mammal or bird to irradiation-detoxified lipopolysaccharide derived from microbial and/or fungal endotoxin.

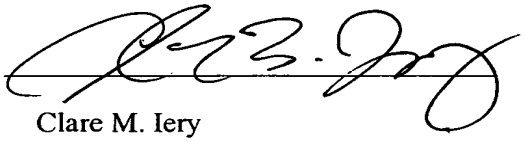
As noted in detail above, Applicants submit that the combination of Tulic et al in view of Matricardi et al and Bertók do not teach, suggest or recognize a process for inhibiting development of an allergic disease comprising exposing a neonatal or immature mammal or bird to irradiation-detoxified lipopolysaccharide derived from microbial and/or fungal endotoxin as defined by the claims. In addition, Applicants find no teaching, suggestion or reference in Tulic et al in view of Matricardi et al and Bertók for modifying the disclosures therein to arrive at the claimed invention. The teachings of Liu et al do not overcome these deficiencies. Liu et al disclose a review of recent studies on endotoxin exposure. However, Liu et al fail to teach, suggest or recognize the use of irradiation detoxified LPS for decreasing allergy sensitization in a neonatal or an immature mammal or bird.

References relied upon to support a rejection under 35 U.S.C. §103 must provide an enabling disclosure, i.e., they must place the claimed invention in the possession of the public, *In re Payne*, supra. As noted above, Applicants find no teaching, suggestion or reference in Tulic et al in view of Matricardi et al and Bertók and further in view of Liu et al of a process for inhibiting development of allergic disease comprising exposing a neonatal or immature mammal or bird to irradiation-detoxified lipopolysaccharide derived from microbial and/or fungal endotoxin as recited by the claims. In addition, Applicants find no teaching, suggestion or reference in Tulic et al in view of Matricardi et al and Bertók and further in view of Liu et al for modifying the disclosures therein to arrive at the claimed invention. In view of the failure of Tulic et al in view of Matricardi et al and Bertók and further in view of Liu et al to teach, suggest or recognize the process for inhibiting development of allergic disease as recited by the claims, the references do not support a rejection of claims 1 and 13 under 35 U.S.C. §103.

It is therefore submitted that the claimed processes as defined by claims 1 and 13 are nonobvious over and patentably distinguishable from the teachings of Tulic et al in view of Matricardi et al and Bertók and further in view of Liu et al, whereby the rejection under 35 U.S.C. §103 has been overcome. Reconsideration is respectfully requested.

It is believed that the above represents a complete response to the rejection of the claims under 35 U.S.C. §§103 and 112, first paragraph, and places the present application in condition for allowance. Reconsideration and an early allowance are requested.

Respectfully submitted,

By: 

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